A COMPARATIVE STUDY OF TWO DOSES OF SPINAL BUPIVACAINE WITH FENTANYL IN ELDERLY PATIENTS UNDERGOING ENDOSCOPIC UROLOGIC PROCEDURES

A STUDY OF 75 CASES

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE
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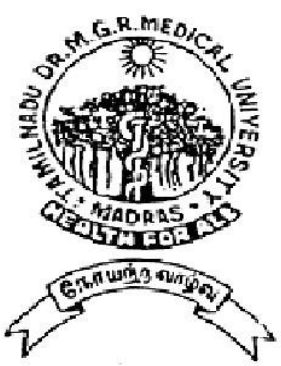

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DR. M.G.R. MEDICAL UNIVERSITY
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BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled **"A COMPARATIVE STUDY OF TWO DOSES OF SPINAL BUPIVACAINE WITH FENTANYL IN ELDERLY PATIENTS UNDERGOING ENDOSCOPIC UROLOGIC PROCEDURES"** is bonafide record work done by **Dr. R.GANESAN** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfillment of University regulation for MD, Branch X – Anaesthesiology.

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DECLARATION

I **Dr.R.GANESAN** solemnly declare that this dissertation titled **"A COMPARATIVE STUDY OF TWO DOSES OF SPINAL BUPIVACAINE WITH FENTANYL IN ELDERLY PATIENTS UNDERGOING ENDOSCOPIC UROLOGIC PROCEDURES"** has been done by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of Doctor of Medicine degree Branch –X (Anaesthesiology) to be held in March 2009.

Place : Madurai **Dr.R.GANESAN**

Date :

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INTRODUCTION

"The relief of pain purchased is always at a price"

- R.M.Water's

"For all the happiness mankind can gain is not in pleasure but in rest from pain"

- John Dyrden

The aim of the anaesthesiology as a science is the removal of pain temporarily have been started initially with pain relief for surgeries, extending now to post operative pain relief and relief from chronic pain and cancer pain.

Spinal anaesthesia plays an important role of alleviating pain intraoperatively, extending into post operative period also.

The entry of corning's needle in 1885 into subarachnoid space paved the way for the greatest leap into spinal anaesthesia. As a neurologist, corning's objective was to relieve chronic pain in his patients, not to produce operative anaesthesia.

Cocaine was the drug first used experimentally in dogs. In men the first spinal anaesthesia was conducted by "August Bier" on 16.08.1898 with cocaine 3cc as 0.5% solution followed by "Rudolph matas" in America and "Theodore Tuffier" in France.

Spinal anaesthesia is the most frequently employed anaesthetic technique for "TURP" and other cystoscopic urologic procedures. It provides an adequet anaesthesia for the patient and good relaxation of the pelvic floor and perineam for the surgeon. The complication of cystoscopic procedures can be easily recognized because of the patient

is awake. Accidental bladder perforation also is recognized easily if the spinal level is limited to T10 as patient experience abdominal and shoulder pain.

ADVANTAGES:

Change in the mental status in a conscious patient can be detected early.

Sympathetic blockade produced by regional anaesthesia will increase the venous capacitance thereby decreasing the effect of fluid absorption.

Bladder perforation is recognized earlier. Reduced incidence of deep vein thrombosis. Decreased requirement of analgesics in the immediate post operative period.

The demonstration of the opiate receptor in the substantia gelatinosa of the spinal cord (yaksh and Rudy-1976) has created interest in the intrathecal administration of opiates.

The advantages of neuraxial opioids over neuraxial local anaesthetics are that it produces prolonged,intense and selective segmental analgesia without motor blockade and sympathetic dysfunction.

Opioids and local anaestheties administered together have a potent synergistic analgesic effect. Intrathecal opioids enhance analgesia from subtherapeutic dose of local anaesthetic and make it possible to achieve successful spinal anaesthesia using otherwise inadequate doses of local anesthetic.

Hence the present study has been under taken to combine “Fentanyl” a potent synthetic opioid and “Bupivacaine” a long acting local anesthetic for intrathecal administration to provide anaesthesia for Endoscopic urological procedures in elder patients.

AIM OF THE STUDY

Regional anaesthesia is the most frequently employed anaesthetic technique for TURP and other endoscopic urologic procedures. These patients are mostly elderly with low cardiac reserve. The conventional dose of Bupivacaine may produce haemodynamic instability. The aim of my study is to find out the minimum effective dose of Bupivacaine with 25µg of fentanyl for spinal anaesthesia in elderly patients undergoing endoscopic urologic procedures.

ANATOMY OF SUBARACHNOID SPACE

Subarachnoid block means the temporary interruption of nerve transminssion within the subarachnoid space produced by injection of a local anaesthetic solution into cerebrospinal fluid.

Applied anatomy of vertebral canal:

Vertebral canal extends from foramen magnum to the sacral hiatus. It protects the spinal cord.

The vertebral column comprised 33 vertebrae (7-cervical, 12-thoracic, 5-lumbar, 5-fused sacral and 4-coccygeal) has four curves. Cervical and lumbar curves are convex anteriorly and thoracic & sacral curves are convex posteriorly. The curves of the vertebral column influences the spread of the local anaesthetic in the subarachnoid space.

Each vertebra is composed of a body separated from the adjacent vertebra by intervertebral disc and vertebral and formed by pedicles and laminae, which surround and protect the cord laterally and posteriosly.

The vertebral column is bound together by several ligaments. They are,

1. Supraspinal ligament – passess longitudinally over the tips of the spinous processes from C7 to the sacrum.
2. Interspinous ligament – connects the adjoining spinous processes together.

3. Ligamentum Flavum – Known as yellow ligament, connects the adjacent laminae composed of yellow elastic fibres. They become progressively thicker from above downwards.
4. Posterior longitudinal ligament – It is on the posterior surface of bodies of vertebral.
5. Anterior longitudinal ligament – It runs along the front of the vertebral bodies.

There are seven projections from these vertebral (or) neural arches. They are,

a) Three muscular processes – (2-Transverse processes, 1-spinous process for the attachment of muscle and ligaments).
b) Four articular process – Two upper & two lower which in the lumbar region prevent rotation but allow limited flexion and extension between contiguous vertebrae.

Vertebral canal formed by these structures has deficiencies posteriorly in the midline called inter laminar foramina which enlarge in flexion accessible for the passage of spinal needle. The direction of spinous process determine the direction of spinal needle.

SPINAL CORD:

It is the direct continuation of the medulla oblongata extending from the upper border of the atlas to the first lumber vertebra below which there is leash of nerve roots termed cauda equina. Spinal nerves are 31 pairs totally.

8 – Cervical

12 – Thoracic

5 – Lumbar

5 – Sacral

1 – Coccygeal

Each of the spinal nerve is composed of anterior and posterior roots uniting at the inter vertebral foramina and form a nerve trunk. Membranes covering the spinal cord from without are dura mater, arachnoid mater and piamater. Dura and arachnoid mater end at S_2 level. Piamater is closely applied to the spinal cord.

BLOOD SUPPLY:

It is from the anterior spinal artery which is a branch of vertebral artery and also by a pair of posterior spinal arteries which arise from the posterior inferior carebellar arteries. There is no anastamosis between these arteries.

SPINAL VEINS:

The spinal veins are arranged into anterior and posterior plexus which are draining into vertebral, azygos and lumbar veins.

CEREBROSPINAL FLUIDS:

This is an ultrafiltrate of the blood plasma from choroids plexus of the lateral ventricles with a pH of 7.32 (7.27-7.37)

It is a clear, colourless fluid found in the cranial and spinal subarachnoid spaces and in the ventricle of the brain.

The total volume of CSF in an average adult ranges from 120-150ml of which 25-35ml is in the spinal subarachnoid space.

Composition of cerebrospinal fluid:

Specific gravity	-	1.006 (1.003-1.009) at 37^0C
Pressure	-	60-80mm of water
Pco_2	-	48mmHg
$HCo3^-$	-	23meq/l
Na^+	-	133-145meq/l
Ca^+	-	2-3meq/l
$Po4^-$	-	1.6mg/dl
Mg^+	-	2-2.5mg/l
cl^-	-	15-20weg/l
Protein	-	23-38mg/dl
Sugar	-	45-80mg/dl
Lymphocytes	-	0-5cells/cmm

An important factor that determine the spread of drug in cerebrospinal fluid is the specific gravity of the drug in relation to that of cerebrospinal fluid (Baricity) which is 1.003-1.009. Hyper baric solution is one which is denser than CSF at 37^0C.

PHYSIOLOGY OF SUBARACHNOID BLOCK

Subarachnoid block implies the temporary interruption of nerve transmission within the subarachnoid space by injections of local anaethetics. The blockade of nerve fibres occur in the order of Temperature, Pain, proprioceptive and then motor fibres.

FACTORS INFLUENCING BLOCK HEIGHT:

a - Site of injection

b - Angulation of needle

c - Characteristic of local anaesthetic

i) Density of local anaesthetic

ii) Specific gravity

iii) Baricity

d - Dose of local anaesthetic

e - Position of the patient during and after injection

f - Anatomic configuration of spinal column.

g - Patient height (at extrems)

h - Volume of cerebrospinal fluid

i - Reduced cerebrospinal fluid with increased intra abdominal pressure (eg. Pregnancy)

a) Effects on Cardio Vascular System:

Most important physiological responses to subarachnoid block involve cardio vascular system due to combined effect of autonomic denervation, higher level of neural block, added effect of vagal innervation.

Local anaesthetics and vasoactive substances administered in small doses intrathercally leads to direct cardiovascular effect.

Level of sympathetic denervation determines the magnitude of cardio vascular system responses, but the relationship is neither predictable nor precise.

Sympathetic denervation produces arterial and more physiologically important arteriolar dilatation and vasodilatation in the venous circulation produces fall in blood pressure.

Due to Bainbridge reflex, the fall in blood pressure is associated with bradycardia, blockade of cardiac sympathetic fibre from T1-T4 is an additional factor that causes bradycardia.

b) Effects on Respiratory System:

Respiration is not depressed normally. High spinal can cause paralysis of intercostals muscles but resting tidal volume, maximum inspiratory volume, respiratory

rate, ABG, negative intrapleural pressure and also the phrenic nerve are unaffected. Hypoxia may accompany hypotension and is corrected by oxygen administration via face mask.

c) Gastro Intestinal Effect:

Preganglionic fibres from T_5-L_1 are inhibitory to gut. So in sympathetic blockade the small intestine contracts with relaxed sphincters and peristalsis remains normal. Handling of viscera causes discomfort and brady cardia since vagus is not blocked.

d) Hepatic and Renal Effects:

The hepatic blood flow decreases and is directly proportional to the decrease in blood pressure. There may be normal hepatic oxygen extraction. Renal blood flow is maintained by autoregulation and does not decrease till mean arterial pressure goes below 50mmHg.

e) Genito Urinary System:

Sphincters of bladder are not relaxed, and tone ureter are not greatly altered. Urinary retension occurs. Penis is often engorged, and erigentes (S2, S3). Uterine tone is unchanged in pregnancy. In the absence of hypotension spinal anaesthesia has got no

effect on the progress of labour and uterine blood flow.

f) Metabolic and hormonal effect:

Spinal anaesthesia bocks hormonal and metabolic responses to nociceptive stimuli arising from the operative site. It minimizes the rise in blood sugar, coritsol, catecholamines renin and aldosterone release associated with stress. Post operative negative nitrogen balance and secretion of antidiuretic hormone are inhibited.

g) Thermo Regulation:

Hypothermia results from heat loss to the cold environment due to vasodilatation.

ANATOMICAL AND PHYSIOLOGICAL ANAESTHETIC IMPLICATIONS IN ELDER PATIENTS

There is no standard definition of elderly, but it is often arbitrarily taken as morethan 65 years. They have an increased risk of morbidity and mortality associated with anaesthesia and surgery due to physiological changes of aging.

a) Cardiovascular System:

- 50-65% of patients have cardiovascular disease.
- Reduction in ventricular compliance due to myocardial fibrosis and wall thickening.
- Systolic hypertension and widened pulse pressure
- Autonomic responses decreases.
- Increased capillary permeability leading to pulmonary oedema.

b) Respiratory System:

- Ventilatory responses to hypoxia and hypercarbia decreases.
- Oxygen consumption and carbondioxide production fall by 10-15% by the 7^{th} decades.
- Lung compliance increases, chest wall compliance decreases. Total thoracic compliance decreases.
- Closing volume increases.

- Airway protective reflexes decreases leading to pulmonary aspiration.
- In edentulous patients face mask seal way be difficult.

c) Renal System:

- Decreased Glomerular filtration rate, decreased creatinine clearence, tubular function reduces leading to reduced concentrating ability.
- Clearance of renally excreted drugs are reduced necessitating dose adjustments.

d) Hepatic System:

- Cellular function is relatively well preserved in healthy patients.
- Hepatic mass and hepatic blood flow decreases.

e) Central Nervous System:

- Brain size and mass decreases, cortical atrophy, dementia affects 10% of patients over 65 years of age.
- They require lower dose of opioids and sedatives.
- Pain threshold may be increased.
- Post operative cognitive dysfunction is common.
- The thirst response to reduced extra cellular fluid volume and increased plasma osmolality is reduced in the elderly, increasing suseebtibility to fluid depletion.

f) Pharmacology:

- Total body water is reduced, fat is increased. Arm brain circulation time is prolonged.
- Reduced plasma albumine concentration decreases dose requirement.
- MAC of inhaled agents decreased.
- Risk of Gastro intestinal tract bleed and acute renal failure due to nonsteroidal anti inflammatory drugs are increased.

g) Thermoregulation:

Temperature regulation is impaired increasing the risk of hypothermia.

h) Endocrine:

Glucose loading is poorly tolerated.

i) Nutrition:

Nutrition status frequently poor.

j) Haematology:

Hyper coagulability and deep vein thrombosis become more common with advancing age.

ANAESTHETIC IMPLICATIONS OF ENDOSCOPIC UROLOGICAL PROCEDURE

Commonly performing endoscopic urological procedures in Government Rajaji Hospital, Madurai are the following.

a) TURP - 49.5%

b) TURBT - 13.5%

c) Vesicolithotripry - 11%

d) OIU - 17.5%

e) Others - 9%

Neuro anatomy of the penis prostate and urinary bladder:

Organ	Sympathetic	Parasympathetic	Spinal levels of pain conduction
Bladder	T_{11}-T_{12}	S_2-S_4	T_{11}-L_2 (dome) S_2-S_4 (neck)
Prostate	T_{11}-T_{12}	S_2-S_4	T_{11}-L_2 S_2-S_4
Penis and urethra	L_1-L_2	S_2-S_4	S_2-S_4

The afferent carrying sensations of stretch end of bladder are parasympathetic, where as pain, touch and temperature sensations are carried by the sympathetic nerves. Sympathetic fibres are predominantly α – adrenergic in the bladder base and urethra and β – adrenergic in the bladder dome and lateral wall.

The majority of patients are undergoing procedure for Benign prostatic hypertrophy. The incidence increases over 60 years of age.

Spinal anaesthesia works well for rigid cystoseopic procedures, and is commonly used for Trans urethral resection of prostate. Sensory supply to the bladder is from T_{11} & T_{12} and urethra, prostate and bladder neck is from S_2-S_4. So block upto T_{11} is necessary for TURP Surgery.

Complications of TURP Surgery:

Bladder distension due to large volume of irrigant fluid used in cystoscopic procedure is a potent stimulant to produce autonomic hyper reflexia. The complications of TURP surgery are mainly due to irrigation fluid used.

i) TURP syndrome

ii) Haemorrhage

iii) Perforation of Bladder

iv) Hypothermia

v) Transient Bacteremia, Septicemia

vi) Transient Blindness

vii) Hyper ammonimia

TURP:

Combination of fluid over load and hyponatremia due to large volume of irrigation fluid absorbed via open venous sinuses.

About 20ml/mt and an average patients absorb a total of 1-1.5 litres. Amount of absorption depends on pressure of infusion venous pressure and duration of procedure.

Clinical Features:

- Restlessness, head ach, Tachypenia, respiratory distress, hypoxia, nausea, vomiting, visual disturbance, confusion, convulsions & coma.
- Pulmonary oedema, Heart failure, cerebral oedema and hyponatremia.

Diagnosed by serum sodium level and arterial blood gas analysis:

Treatment:

- Reassure the patient
- Terminate the surgery as soon as possible.
- Switch over to normal saline for bladder irrigation.
- Administer injection furosemide 20mg intravenously
- Administer oxygen through face work.
- If the patient develops pulmonary oedema intubate and give positive pressure ventilation. Invasive haemodynamic monitors may be needed.
- Draw arterial blood for arterial blood gas analysis and serum sodium estimation.
- Intra venous hypertonic saline (3% (or) 5%) may be needed if the hyponatremia present in the rate of 100ml/hour.
- Anti convulsant if the patient develops seizures.
- Transfuse packed red cell if blood loss is more.

PHARMACOLOGY OF DRUGS

a) Bupivacaine:

Bupivacaine is an amide linked local anaesthetic. It is a hydrochloride salt of d(1)-1-butyl 2'6' pipecoloxylidide and is presented as a racemic mixture.

- It was synthesized by EO af Ekenstem.
- First reports of its use was published in 1963 by Telivuo.
- It is derived from Mepivacaine and is very stable compound and may be autoclaved repeatedly.

Pka is 8.1

MW - 288

Protein biuding - 95%

Lipid solubility - 28

Ellimination half life - 210mts

Toxic plasma concentration - >1.5µg/ml

Approximate duration of action - 175mts

Availability:

Ampouls - 0.5% Bupivacaine hydrochloride 4cc

- 0.5% Bupivacaine hydrochloride with dextrose (heavy) 4cc

Vials - 0.25% and 0.5% Bupivacaine hydrochloride 20cc

Dosage - Maximum dosage 3mg/kg body weight.

Uses:

- Spinal anaesthesia
- Epidural anaesthesia
- Caudal anaesthesia
- Continuous epidural anaesthesia
- Peripheral nerve block

Onset time and duration of action

Site of action	Onset (minutes)	Duration (minutes)
Intrathecal	5	180-240
Epidural	15-20	165-225
Brachial plexus	15-20	600

Pharmacokinetics:

Once injected intra thecally, it gets absorbed by the nerve rootlets and results in the desired effect. It is rapidly absorbed from the site of injection, but the rate of absorption depends on the vascularity at the site and presence of vasoconstrictors.

High lipid solubility of bupivacaine makes it easy for nerve and vascular tissue penetration.

80-95% of the absorbed bupivacaive binds to the plasma.

Distribution:

Rapid distribution phase: (α)

In this phase the drug is distributed to highly vascular region $t1/_2$% of α - being

2.7 minutes.

Slow disappearance phase: (β)

In this phase the drug distributes to slowly equilibrating tissues $t1/_2$ of β – being 28mts.

Biotransformation and excretion phase δ

$T1/_2$ of δ is 3.5hours clearance is 0.47 litre/minute.

Biotransformation:

Possible path ways of metabolism of bupivacaine include aromatic hydroxylation and conjugation. Only the N-dealkylated metabolite, N-desbutyl bupivacaine has been measured in blood (or) urine after epidural (or) spinal anaesthesia. Alpha1 acid glycoprotein is the most important plasma protein binding site of bupivacaine and its concentration is increased by many clinical situation including post operative trauma.

Exerction:

It is through the kidney, 4-10% of the drug is excreted unchanged.

Mode of Action:

a) Site of action:

i) The spinal nerve rootlet fine nerve filaments having a large surface area are exposed to the local anaesthetics.

ii) Posterior and lateral aspects of the spinal cord itself.

b) Sodium Channel blockade:

They impede sodium ion access to the axon interior by occluding the transmenbrane sodium channels thus delaying the process of depolarization and axon remains polarized. It is a non-depolarisation blockade.

Pharmacodynamics:

It has got a longer duration of action but a slower onset.

Cardio vascular system:

It reduces cardiac output by reducing the sympathetic tone, by slowing the heart rate and by reducing the venous return, it produces a fall in arterial blood pressure but it is relatively slow and is seldom very profound.

It produces a fall in central venous pressure. It causes an increase in lower limb blood flow. It causes a reduction in incidence of deep vein thrombosis.

Respiratory System:

Spinal blockade seldom, if ever causes respiratory problem.

Gastro intestinal tract:

There is an increase in gastro intestinal motility and emptying of the gastric contents are better.

Toxicity:

Toxicity is related to plasma level of unbound drug and more likely due to an inadverdant intravenous injection. Systemic toxicity reactions primarily involve central nervous system and cardio vascular system. The blood level required to produce central nervous system toxicity is less than that required to produce circulatory collapse.

Central Nervous System Toxicity:

Initial symptom includes feeling of light headedness and dizziness, followed by visual and auditory disturbances. Objective signs are excitatory and includes shivering, muscle twitching and tremor. Ultimately generalized tonic, clonic seizures occurs.

Cardiovascular System Toxicity:

The rate of depolarization in fast conducting tissue of purkinje fibres and ventricular muscle is decreased. The rate of recovery of bupivacaine induced block is slower than that of lignocaine. Extremely high concentration of the drug causes sinus brady cardia and cardiac arrest.

b) Pharmacology of Fentanyl:

Fentanyl is N-1 (1-phenethyl-4, piperidylpropionalide citrate)

It is a synthetic narcotic agonist that is related to phenyl piperidine derivative.

Fentanyl is 75-to-125 times more potent than morphine as an analgesic agent. It has got a rapid onset and a shorter duration of action.

Availability:

Ampoules - 2ml containing 100µg

- 10ml containing 50µg/ml

Lollipop - for paedatric use

Patches - Transdermally delivering a dose of 75 to 100µg/hour

Routs of Administration:

Fentanyl is the only opioid available for various forums of administration.

It can be used by the following routs:

- Intramuscular
- Intravenous
- Neuroxial – Spinal, epidural administration for intra and post operative analgesia.
- Transdermal – applied before the induction of anaesthesia and left in place for 24 hours. It can reduce the amount of parenteral opioid requirement for post operative analgesia.
- Tansmucosal: to decrease the anxiety and to facilitate induction of anaesthesia especially in children.

Dosage:

Intramuscular - 1-2µg/kg

Intravenous - 2-20µg/kg – Intravenous with inhaded anaesthetics.

50-150µg/kg – sole anaesthetic agent

Intrathecal - 0.25 – 0.5µg/kg

Epidural - Bolus dose - 1µg/kg

Continuous infustion – 30-300µg/hour

Onset time and duration of action

Routs of administration	**Onset time (minutes)**	**Duration of action (minutes)**
Intramuscular	7-8mts	1-2hour
Intravenous	Immediate	0.5-1hour
Epidural	10mts	2-3hours

Pharmacokinetics:

MW - 528

Pka - 8.4

Plasma protein binding - 84%

$t1/_2 – \alpha$ - 1-2mts

$t1/_2 – \beta$ - 10-30mts

$t1/_2 – g$ - 2-4mts

Being a highly lipophilic opioid the vascular uptake and rapid circulation to brainstem is more and the rostral spread is of smaller magnitude. These kinetics of Fentanyl is in contradiction to morphine and clinically produces rapid onset shorter duration of action, early but not delayed respiratory depression.

Once the Fentanyl is systemically absorbed, it is rapidly redistributed to inactive tissue sites such as fat and skeletal muscles with an associated decline in plasma concentration. The lungs also serve as a large inactive storage sites, with an estimated 75% of the initial Fentanyl dose undergoing first pass pulmonary uptake.

Fentanyl is extensively metabolized by dealkylation, hydroxylation and amide hydrolysis to inactive metabolites including nor fentanyl and desporprionyl nor fentanyl that are excreted in the bile and urine.

The pharmacokinetics of Fentanyl can be described as three compartment model with a distribution time of 1.7 minutes redistribution of 13 minutes and a terminal half time of 219 minutes. The volume of distribution is 42ml/kg.

Gastric acidity can ionize Fentanyl and prevents its systemic absorption and once the acidity is neutralized the systemic absorption can increase the plasma Fentanyl concentration. Entero hepatic circulation of Fentanyl can explain the delayed respiratory depression seen in some cases.

MODE OF ACTION:

Opioid Receptor:

Opioids act as agonist at stereospecific opioid receptors at presynaptic sites in the central nervous system (principally the brainstem and spinal cord) and outside the central nervous system in peripheral tissues.

Mu, Kappa, Sigma, Delta and Epsilon are the different opioid receptors distributed in the supraspinal areas (periaqueductal grey mater, caudate, striatum and putamen) and the spinal cord (highest density in the substantia gelatinosa)

Fentanyl acts on the μ receptor in the supraspinal areas and on kappa and delta receptors in the spinal cord producing spinal analgesia.

Intra thecally administrated Fentanyl gets attached to the spinal opioid receptors situated densly in the substantia gelatinosa and systemic absorption of the Fentanyl can lead to supraspinal receptors binding and its effects.

Investigation suggest that different receptors are existing for different opioids. These receptors are distributed throughout the central nervous system and other parts of the brain like paleothalamic pathway, limbic system, medial thalamic nuclei, aqueductal grey mater, reticular formation, periventricular areas of medulla, substantia gelatinosa of spinal cord, lamina I & II of spinal cord.

Opiate receptors are proteolipids which can bind to both agonists and antagonists.

CLASSIFICATION OF OPIOID RECEPTORS

'μ' Receptor:

Stimulation of this receptor causes supraspinal analgesia, euphoria, respiratory depression and physical dependence. This receptor is sterospecific and naloxone sensitive. Endogenous ligand for μ receptor is endorphin and exogenous ligand is morphine, the selective antagonist being naloxone.

μ_1 receptor:

Stimulation of this receptor causes supraspinal analgesia and physical dependence.

μ_2 receptor:

Stimulation of this receptor causes respiratory depression, inhibition of gastro intestinal tract motility and cardiovascular system effects.

K receptor:

Ketocyclozocine is the prototype agonist. Stimulation causes spinal analgesia, sedation, miosis, physical dependence and inhibition of ADH secretion. Endogenous ligand is dimorphine and the selective antagonist is naloxone.

'δ' receptor:

This receptor has high affinity for adrenocorticotrophic peptide harmone.

Function is not clear but it may be responsive for modulation of activity of 'G' receptors.

It may cause spinal analgesia and respiratory depression. It is not sterospecific and is naloxone insensitive.

'σ' receptor:

Stimulation of this receptor cause dysphonia, hallucination, mydriasis and respiratory depression.

'ε' receptor:

This receptor is not well characterized at present and it may be responsible for the stress response to pain. Endogenous ligand is p-endorphin and the autagonist being naloxone.

Opioid receptor in the limbic system and hypothalamous are related to the emotional components of pain. Encephalin containing receptors are found in Meissener's plexus of duodenum, which probably affects gastro intestinal motility. Opiate receptor are found in large numbers in the area postrema, which contain chemo receptor trigger zone, the site where opioids are thought to induce nausea and vomiting.

Mechanism and Site of Action:

Recent studies now point to the dorsal horn of spinal cord is the site of action of

spinal opiate based upon ionatophoretic and micro injection data. Radio labeled morphine (or) Fentanyl showed a strong focus of activity on the substantia gelatinosa.

Opiate receptors are located both presynaptically at the terminal of primary sensory afferents entering the dorsal horn and on the dentrites of post synaptic membranes.

Presynaptically opiate peptides inhibit the release of substance-P, glutamate and other neurotransmitter like acetylcholine nor adrenaline, dopamine from sensory neurons. They also act post synaptically by decreasing the excitatory post synaptic potentials induced by persistant afferent stimulation.

Intraoperatively subarachnoid narcotics potentiate the antinociception provided by the local anaesthetic agents. There is enhancement of comfort and also the visceral manipulation are better tolerated.

Fentanyl also binds to M3 muscarinic receptors in the heart leading to bradycardia which can be prevented by giving atropine to the patient.

Fentanyl also antagonizes 5-HT level in the brain, there by potentiating the analgesic activity of other opioids.

PHARMACEODYNAMICS OF FENTANYL:

i) Cardiovascular System:

It produces bradycardia by binding to M3 receptors. It slows AV node conduction and prolongs PR interval.

ii) Respiratory System:

It can cause early respiratory depression peak effect is noted 5-15 minute following intravenous injection. Very rarely delayed respiratory depression can occur.

iii) Musculo Skeletal System:

It may cause muscle rigidity, particularly involving the muscles of the chest wall.

Skeletal muscle movements of various groups in the extremities, in the neck and in extra-ocular muscles have been reported during induction of anaethesia. This effect is related to the dose and speed of injection.

iv) Central Nervous System:

It produces euphoria, sedation and miosis. It will not interfere with evoked potential monitoring.

v) Gastro Intestinal Tract:

It causes nausea, vomiting and biliary spasm.

ADVERSE EFFECTS:

a) Respiratory Depression:

Various studies have showed that respiratory depression may occur after any Opioid irrespective of its routs of administration.

b) Urinary Retension:

It is likely to interact with Opioid receptors located in sacral segments of spinal cord. This in turn promots inhibition of sacral parasympathetic nervous system outflow which causes detrusor muscle relaxation and an increase in maximum bladder capacity leading to urinary retention.

c) Pruritus:

Most common side effect is pruritus. The incidence is 0-100%. It may be generalized (or) localized to the face, neck and upper thorax. The sensation appears around (or) just after the development of analgesia by epidural (or) intra thecal Opioids.

d) Nausea and Vomiting:

Intra operative incidence is 30%. It may be due to the cephalad migration of drug and subsequent interaction with Opioid receptors in vascularized area postrema.

e) Hypotension:

Intra thecal pethidine and sufentanil cause hypotension. Where as intrathecal Fentanyl does not cause this effect. The mechanism is not known.

f) Delayed gastric emptying:

This effect is mediated at the spinal level and hence neuroxial opioids are not exempt from this effect.

g) Other side effects:

- Chest wall muscle rigidity
- Apnoea
- Bradycardia
- Diaphoresis
- Emesis
- Dizziness
- Blurred vision

Over Dosage and its Treatment:

The manifestations of Fentanyl over dosage are an extension of its pharmacological actions

Effects	Treatments
1. Hypoventilation	Oxygen therapy assisted (or) controlled ventilation
2. Severe respiratory depression	Nalaxone
3. Hypotension	Parenteral fluid therapy
4. Pruritus	Chlorpheniramine maleate

HISTORY AND REVIEW OF LITERATURE

History:

SUB ARACHNOID BLOCK:

In 1885, J.Leonard corning a New York neurologist first used cocaine experimentally in dogs. In men the first spinal anaesthesia was conducted by August Bier on 16.08.1898 with cocaine 3cc as 0.5% solution.

It was followed by Rudolf matas in America and Tuffier in France.

Bupivacaine:

It was synthesized in Sweden by Ekenstam and his colleagues in 1957 and used clinically by L.J.Telivl. Jo in 1963.

Intrathecal Opioids:

Gate control theory of pain (1965) by Melzack and Wall focused the attention on importance of dorsal horn of spinal cord in the modulation of pain.

In 1973, Pert (and) Snyder identified the specific opiate receptors in the substantia gelatinosa of dorsal horn of spinal cord.

In 1976, spinal effects of intra thecal opiates in animals were demonstrated by Yaksh and Rudy.

In 1977, Wang, Naurs and Thomas studied the effect of intra thecal morphine in men with intractable pain of lowerlimb due to malignancies invading lumbosacral plexus.

In 1980, Davier et al, identified that respiratory depression with intratheeal morphine was reversed with systemic naloxone without reversing analgesia.

In 1981, Yaksh and Rudy described the action of intrathecal pethidine and morphine in primates by iontophoretic administration of the drugs in to the substantia gelatinosa. They found out high level of opiates binding in substantia gelatinosa indicating the presynaptic action of opiate. Spinal opiates also seemed to cause significant elevation of noeicpetive threshold.

In 1984, Huang HJ, Ishimain T, Yambe studied the use of intrathecal morphine for post operative pain relief.

In 1988, Inagaki. Y, Takeyama E studied the efficacy of post operative pain relief after the use of intrathecal Buprenorphine with local anaesthetic agent and found it to prolong the post operative analgesia.

FENTANYL AND INTRATHECAL ANAESTHESIA:

The increased availability of lipid soluble opioids with shorter latency and demonstration of synergistic effect of opioids when combined with local anaesthetics

have led to the widespread use of neuroxial opioids. The effect of lipophilic agents are better when administered at the level at which analgesia is required. Commonly used opioids are meperidine, Fentanyl and sufentanil.

Mok et al 1984, Intra thecal injection of Fentanyl, sufentanil, alfentanil and nalbuphine have been reported for post operative analgesia with promising results.

Wang, Chen MB et al 1993, This study examined the effect of Bupivacaine administered intrathecally on sympathetic efferent and 'A' delta and 'C' fibre mediated afferent pathways in dogs and the interactions with intrathecal fentanyl. The results showed that intra thecal bupivacaine has no selectivity for the afferent and efferent pathways and intratheeal Fentanyl acts synergistically to enhance the effect of bupivacaine on the afferent pathway without a measurable effect on sympathetic out flow.

Singh, Harbheo, Yang et al 1995, They studied the effect of intrathecal Fentanyl on the onset and duration of hyperbaric bupivacaine induced spinal block in adult male patients undergoing genito urinary surgery. They concluded that Fentanyl 25µg, prolongs the duration of bupivacaine induced sensory block by 28% and increased the post operative analgesia.

Hunt et al reported that addition of Fentanyl 6.25µg to the hyperbaric bupivacaine reduced the intra operative Opioid requirement in patients undergoing caesarean

delivery under sub arachnoid block.

Belzarena et al demonstrated that low dose Fentanyl 0.25µg/kg with bupivacaine 0.5% provided excellent surgical anaesthesia with few side effects. An increased dose of Fentanyl to 0.5µg/kg was associated with an increased incidence of adverse effects in patients undergoing caesarean delivery.

Ce-Ben David et al 1997, By exploring the synergism between intrathecal opioids and local anaesthetics, it may be possible to augment the spinal anesthesia without prolonging the recovery. Based on this fact they have done the study on 50 patients undergoing ambulatory surgical arthroscopy. Implications: Small dose bupivacaine is inadequate for this procedure but the addition of Fentanyl makes it reliable.

Roussel JR et al 1999, they have concluded a study on the effects of intrathecal Fentanyl on duration of bupivacaine spinal blockade for out patient knee arthroscopy and concluded that Fentanyl does not enhance the onset and duration of sensory (or) motor block produced by intratecal bupivacaine. Fentanyl however prolong post operative analgesia and increases the risk of pruritus.

Ben David B, Frankel R et al 2000, They studied the effect of mini dose bupivacaine fentanyl spinal anaesthesia for surgical repair of hip fracture in the aged. The synergism between intrathecal opioids and local anaesthesia may make it possible to achieve reliable spinal anaesthesia with minimal hypotension using a small dose of local

anaesthetic. 20 patients of more than 70 years of age for surgical repair of hip were divided in to 10 patient of group each.

Group A - Received bupivacaine 4mg and Fentanyl 20µg

Group B - Received 10mg of bupivacaine alone.

They concluded that the mini dose combination caused dramatically less hypotension than 10mg bupivacaine and nearly eliminated the need for vasopressor support of blood pressure.

Pramod Patra, Mukul Chandra Kapoor, Trevor Gordon Michael Nair. They studied the effect of low dose bupivacaine with Fentanyl for elderly patients undergoing endoscopic urological procedure. They concluded that the addition of Fentanyl to bupivacaine provide adequate surgical anaesthesia with an ideal peak sensory block height and significantly reduces the duration of both sensory and motor blockade, with no significant adverse effects apart from pruritus, facilitating early discharge of patients. The technique was found suitable for day care endoscopic urologic procedure.

Ben David B, Levin H, Solomon E, et al, studied spinal anaesthesia in ambulatory surgery. The effect of saline dilution was studied. They concluded that the most important determinant of both successful surgical anaesthesia and time until recovery is the dose of local anaesthetic drug.

MATERIALS AND METHODS

After getting the approval from the ethical committee of the department of anaesthsiology, Govt. Rajaji Hospital attached to Madurai Medical College, Madurai. The study was conducted in 75 patients aged 50-75years undergoing elective endoscopic urologic procedures. After getting consent and explaining the procedure details the anaesthetic technique was performed.

EXCLUSION CRITERIA:

- Patient refusal
- ASA III & IV patients
- Post spinal surgeries
- Spinal deformity
- H/o drug allergy

Preoperative preparation:

After routine preoperative assessment as for all elective surgery patients they were premedicated with injection Midazolam 2mg Im 30-45 minutes before surgery.

Patients were randomly divided into three groups.

Group B - Received Inj. 0.5% Bupivacaine 1.5cc

Group FI - Received Inj. 0.5% Bupivacaine 1cc +
Inj. Fentanyl 0.5cc = 1.5cc

Group FII - Received Inj. Bupivacaine 0.8cc+
Inj. Fentanyl 0.5cc+
Sterile water 0.2cc =1.5cc

PROCEDURE DETAILS:

On preoperative visit the patients were explained about the procedure details. Then preoperative baseline parameters like pulse rate, blood pressure, respiratory rate were recorded. Iv line started with 18 gauge intra venous cannula and infused with crystalloids.

Following emergency drugs and equipments were kept ready before anaesthesia intervention.

- Boyles machine with oxygen cylinder
- Oxygen source
- Laryngoscope with various blades
- Airway in all sizes
- Suction apparatus

- Emergency drugs like ephedrine, dopamine, atropine and adrenaline
- Naloxone

Patients were put in right lateral position and with strict aseptic precaution lumbar puncture was done with quinke standard 23 guage spinal needle.

After ensuing free flow of CSF drug was injected as per the group assigned.

The assigned amount of Fentanyl and strile water were taken in sterile tuberculine syringe.

After injection patient were put up in supine position. After attaining adequate peak level of sensory block the patient was put up in lithotomy position. If needed oxygen was given through ventimask.

THE FOLLOWING PARAMETERS WERE RECORDED

1. Time of highest level of sensory block achieved by pin prick and temperature.
2. Degree of motor blockade assessed by using bromage scale.
3. Pulse rate, Blood pressure, respiratory rate, spo_2 were monitored every 2 minutes for 10 minutes and every 5 minutes till the end of surgery.
4. Any discomfort like nausea, vomiting, pruritus and shivering.
5. Hypotension is said to have occurred if there was 30% fall from base line and was treated with 100% O_2, Intravenous fluid bolus and Inj. Ephedrine in incremental

doses.

6. Bradycardia – if present was treated with Inj. Atropine.
7. Sedation score
8. Incomplete sensory block
9. Post operative observation:
    a. Duration of procedure
    b. Level at the end of surgery
    c. Duration of post operative analgesia
    d. Two segment regression time (i.e. the time taken to decrease from maximum sensory level by two segments from initial level is noted)

SEDATION SCORE:

Brain and Ready sedation score was employed

0 - Fully awake

1 - Drowsy

2 - Drowsy but arousable on touch (or) call

3 - Drowsy but arousable on deep stimuli

4 - Somnolent

In the post operative period total duration of analgesia was taken as that period from time of subarachnoid block till patient requirement of analgesic medicine.

Pain was evaluated using **VISUAL ANALOG SCALE.**

0-1 - Excellent

2-4 - Good

5-6 - Fair

7-8 - Poor

9-10 - No relief

Pain score >6 – supplementary analgesia given.

MOTOR BLOCK WAS ASSESSED BY BROMAGE SCALE

0 - Full flexion of knees, feet, able to lift the extended leg

1 - Unable to lift the extended leg. Just able to flex the knees and full flexion of feet possible

2 - Unable to flex the knees but flexion of feet possible.

3 - Unable to move the leg (or) feet

also in the post operative period all patients were followed up for any complications like post operative nausea, vomiting, pruritus, hypotension and respiratory

depression.

Statistical significance was brought out by ANOVA table.

RESULTS

A. PROFILE OF CASES STUDIED

Table 1 : Age distribution

Age group	Cases in Group B		Group F1		Group F11	
	No.	**%**	**No.**	**%**	**No.**	**%**
Less than 50 years	-	-	-	-	-	-
50– 54 years	5	20	7	28	5	20
55 – 59 years	8	32	1	4	2	8
60 – 64 years	4	16	10	40	7	28
65 – 69 years	5	20	5	20	6	24
70 years & above	3	12	2	8	5	20
Total	25	100	25	100	25	100
Mean	60.2		60.2		62.4	
S.D.	7.0		6.6		8.2	
'p'	0.5025 Not significant					

Table 2 : Sex distribution

Sex	Cases in					
	Group B		Group F1		Group F11	
	No.	%	No.	%	No.	%
Males	23	92	24	96	22	88
Females	2	8	1	4	3	12

Table 3 : History of illness

Illness	Cases in					
	Group B		Group F1		Group F11	
	No.	%	No.	%	No.	%
D.M.	5	20	1	4	4	16
H.T.	3	12	5	20	3	12
I.H.D.	1	4	1	4	-	-
COPD	-	-	2	8	1	4
Others	7	28	3	12	2	8

Table 4 : Baseline data

Parameter	Cases in						'p'
	Group B		Group F1		Group F11		
	No.	%	No.	%	No.	%	
Pulse Rate	87.1	7.3	82.1	6	81.7	7.4	0.0681 Not Significant

Respiratory Rate	14.52	3.23	14.12	2.09	14.12	2.24	0.9714 Not Significant
Systolic B.P.	120.4	14.85	123.2	11.08	124.4	8.7	0.2972 Not Significant
Diastolic B.P.	77.2	7.4	79.2	7	78	7.1	0.4766 Not Significant

B. INTRA OPERATIVE OBSERVATION

Table 4 : Maximum Sensory Level

Maximum Sensory Level	Cases in					
	Group B		Group F1		Group F11	
	No.	%	No.	%	No.	%
T6	1	4	-	-	-	-
T7	2	8	-	-	-	-
T8	1	4	5	20	2	8
T9	9	36	10	40	4	16
T10	10	40	8	32	19	76
T11	2	8	2	8	-	-
Total	25	100	25	100	25	100
Mean	9.24		9.28		9.68	
S.D.	1.2		0.89		0.63	
'p'	0.1243 Not Significant					

Table 5 : Time of Maximum Sensory Level

Maximum Sensory Level	Cases in		
	Group B	Group F1	Group F11
Range	5-9	5-8	5-7
Mean	7.0	6.0	6.16
S.D.	1.15	0.91	0.8
'p'	**0.0021 Significant**		

Table 6 : Grading of Motor Block

Motor Block Grade	Cases in					
	Group B		Group F1		Group F11	
	No.	%	No.	%	No.	%
1	-	-	-	-	1	4
2	1	4	2	8	9	36
3	13	52	18	72	14	56
4	11	44	5	20	1	4
Total	25	100	25	100	25	100
Mean	2.4		2.12		1.6	
S.D.	0.58		0.53		0.65	
'p'	**0.0001 Significant**					

B. INTRA OPERATIVE HAEMODYNAMIC CHANGES

Table 7 : Changes in Pulse Rate

Pulse Rate	Cases in						'p'
	Group B		Group F1		Group F11		
	No.	%	No.	%	No.	%	
Base line	87.1	7.3	82.1	6	81.7	7.4	**0.0681 Not significant**
At 5 minutes	88.8	7.2	83.1	7.6	86.2	8.8	**0.0281 Significant**
At 10 minutes	89.3	7.1	85	5.5	85.5	5.5	**0.0081 Significant**
At 15 minutes	89.3	6.3	84.7	5.3	85	4.8	**0.0019 Significant**
Changes at							
5 minutes	1.72	11.71	0.96	7.93	4.48	8.54	0.5674 Not significant
10 minutes	2.16	12.12	2.92	6.53	3.8	7.75	0.9459 Not significant
15 minutes	2.16	11.23	2.6	6.71	3.24	7.77	0.9525 Not significant
% of change at							
5 minutes	2.97	14.52	1.49	9.97	5.92	10.73	0.4771 Not significant
10 minutes	3.53	14.74	3.95	8.62	5.33	10.33	0.9385 Not significant
15 minutes	3.47	13.87	3.59	8.88	4.69	10.43	0.9638 Not significant

Table 8 : Changes in Systolic B.P.

Systolic B.P.	Cases in						'p'
	Group B		Group F1		Group F11		
	No.	%	No.	%	No.	%	

Base line	120.4	14.85	123.2	11.08	124.4	8.7	0.2972 Not Significant
At 5 minutes	102.64	17.77	117.2	12.08	117.6	8.79	**0.0012 Significant**
At 10 minutes	110.3	10.69	116.4	9.95	115.6	11.58	0.0961 Not Significant
At 15 minutes	111.2	10.92	116.4	9.95	118.4	9.43	0.0501 Not Significant
Changes at							
5 minutes	-17.76	14.45	-6	10	-6.8	8.52	**0.0006 Significant**
10 minutes	-10.08	10.96	-6.8	7.48	-8.8	10.13	0.4863 Not Significant
15 minutes	-9.2	8.62	-6.8	9.45	-6	7.07	0.3769 Not Significant
% of change at							
5 minutes	-14.62	11.63	-4.65	7.94	-5.28	6.63	**0.0002 Significant**
10 minutes	-7.84	8.59	-5.35	6.08	-7.04	8.11	0.2302 Not Significant
15 minutes	-7.19	6.63	-5.2	7.46	-4.7	5.57	0.1931 Not Significant

Table 9 : Changes in Respiratory Rate

Respiratory Rate	Cases in						'p'
	Group B		Group F1		Group F11		
	No.	%	No.	%	No.	%	
Base line	14.52	3.23	14.12	2.09	14.12	2.24	0.9714 Not Significant
Intra operative	14.08	2.48	13.4	1.68	14.56	2.63	0.2382 Not Significant
Change	-0.44	2	-0.72	2.01	0.44	1.64	0.1167 Not Significant
% of change	-1.44	13.27	-3.95	13.33	3.44	11.23	0.1044 Not Significant

Table 10 : Complications

Complications	Cases in					
	Group B		Group F1		Group F11	
	No.	%	No.	%	No.	%
Incomplete Sensory Block	-	-	-	-	2	8
Nausea / Vomiting	-	-	-	-	-	-
Pruritus	-	-	6	24	4	16
Any discomfort	-	-	-	-	-	-

Incomplete sensory block was present in 8% of patients in Group FII

Table 11 : Sedation Score

Sedation Score	Cases in					
	Group B		Group F1		Group F11	
	No.	%	No.	%	No.	%
0	22	88	2	8	3	12
1	3	12	16	64	16	64
2	-	-	5	20	6	24
3	-	-	2	8	-	-
Total	25	100	25	100	25	100
Mean	0.12		1.28		1.12	
S.D.	0.33		0.74		0.6	
'p'	0.0001 Significant					

Sedation Score was more in Fentanyl group

Table 12: Duration of Procedure

Duration of Procedure in minutes	Group B	Group F1	Group F11
Range	20 – 60	20 – 60	25 – 75
Mean	32	39.4	54.2

S.D.	10.2	10.3	12.7
'p'	**0.0001** **Significant**		

Table 13: Two seg. regression time

Two seg. regression time in minutes	**Group B**	**Group F1**	**Group F11**
Range	78 – 95	77 – 117	69 – 101
Mean	85.8	95.7	82.5
S.D.	5.74	9.13	8.85
'p'	**0.0001** **Significant**		

Two segment regression time was significantly prolonged in group-FI ('P' 0.0001)

Table 14: Duration of post operative analgesia

Duration of post operative analgesia in minutes	**Group B**	**Group F1**	**Group F11**
Range	85 – 108	92– 127	75 – 105
Mean	95.4	105.8	90.4
S.D.	4.4	9.3	7.8
'p'	**0.0001** **Significant**		

Duration of post operative analgesia was significantly prolonged in Group FI

Statistical Tools (To be included at the end of Materials and Methods)

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2002).**

Using this software, range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

OBSERVATION AND RESULTS

In this randomized single blinded study conducted in 75 patients, the subjects were allocated in to three groups.

Group B - Received Inj. 0.5% Bupivacaine 1.5cc

Group FI - Received Inj. 0.5% Bupivacaine 1cc+ 25µg of Inj. Fentanyl

Group FII - Received Inj.0.5% Bupivacaine 0.8cc + Inj. Fentanyl 25µg + Sterile water 0.2cc

DEMOGRAPHIC DATA:

All 3 groups were comparable in age, sex, duration and nature of surgery.

HIGHEST DERMATOMAL LEVEL:

Maximum level achieved

Group B - T_9

Group FI - T_9

Group FII - T_{10}

TIME OF MAXIMUM SENSORY LEVEL:

Group B - 7mts with SD of 1.15

Group FI - 6mts with SD of 0.91

Group FII - 6.16mts with SD of 0.8

GRADING OF MOTOR BLOCK:

Group B - 44% of patients had grade 3

52% of patients had grade 2

4% of patients had grade 1

Group F1 -20% of patients had grade 3

72% of patients had grade 2

8% of patients had grade 1

Group F11-4% of patients had grade 3

56% of patients had grade 2

36% of patients had grade 1

4% of patients had grade 0

HAEMODYNAMIC VARIABLES:

With regard to blood pressure more than 30%free from the base line value was considered hypotension.

In Group B - 25% of patients had significant hypotension

In Group FI - There was no significant fall in blood pressure

In Group FII - There was no significant fall in blood pressure

Considering three groups plain bupivacaine group had significant haemodynamic impairment when compared to Fentanyl group, and they required intravenous fluids, Inj. Ephedrine and oxygen supplementation. Of the 2 fentanyl groups none had significant changes in haemodynamic parameters.

INCOMPLETE SENSORY BLOCK:

In group FII 8% of patients had incomplete sensory block and they felt discomfort during the surgical procedure. They were supplemented with Inj. Propofol 1mg/kg + Inj. Fentanyl 1µg/kg intravenously and oxygen.

SEDATION:

Intra operative sedation was excellent in group FI & Group FII

In Group B - 88% had sedation score of 0

12% had sedation score of 1

In Group FI - 8% had sedation score of 0
64% had sedation score of 1

20% had sedation score of 2

8% had sedation score of 3

In Group FII - 12% had sedation score of 0

64% had sedation score of 1

24% had sedation score of 2

TWO SEGMENT REGRESSION TIME:

Duration of analgesia as measured by two segment regression time in Group B was 85.8mts with SD of 5.74

Group FI was 95.7mts with SD of 9.13

Group FII was 82.5mts with SD of 8.85

TOTAL DURATION OF ANALGESIA:

Total duration of pain free interval in

Group B was 95.4mts with SD of 4.4

Group FI was 105.8mts with SD of 9.3

Group FII was 90.4mts with SD of 7.8

COMPLICATIONS:

Nausea and vomiting was not found in all groups.

Pruritus developed in

Group FI - 24% of patients

Group FII - 16% of patients

All responded to Inj. Chlorpheniramine maleate Im.

DISCUSSION

The pain we perceive after a burn, bite (or) pinch is readily identifiable but difficult to define because it is differently perceived at different threshold.

Pain is defined as psychical adjunct of protective reflex – by sherington in 1906.

The international association of society for pain (IASP) defined it as "An unpleasant sensory and emotional experience associated with actual (or) potential tissue damage (or) described in terms of such damage"

The use of opioids to control pain exists even in ancient history and opioids are still the primary analgesic chosen for sever pain.

Advantage of intrathecal administration of narcotics are

- Easier administration at the time of induction of anaesthesia.
- Very small dose and there fore reduced blood concentration of Opioid and reduced risk of complications.

Because most of the cystoscopic urological procedures are performed under subarachnoid block the utility and safety of intrathecal opioids for pain relief is of important clinical concern.

This study combined Fentanyl with low dose of local anaesthetic aimed to delineate the safe limit of local anesthetic that could be added to Fentanyl for elderly patients under going endoscopic urological procedures without much untoward effect.

INTRA OPERATIVE COMFORT:

Addition of Opioid aids in relieving the discomfort that could be casued by visceral handling.

-8% of patients in group FII felt discomfort during the surgery and they needed intravenous analgesic supplement otherwise all patients were comfortable.

- All patients in fentanyl group were comfortable in lithotomy position though the motor block was low

HAEMODYNAMICS:

The haemodynamics were stable in Fentanyl group than plain bupivacaine group (P 0.0012) 28% of group B had hypotension.

This observation is similar to A.Kararmaz et al.

SEDATION:

In Fentanyl group most of the patients were sedated well with sedation score of more than 1 (P 0.00013) than plain bupivacaine group.

PRURITUS:

The incidence of pruritus in group FI is 24% and in group FII is 16%. Nausea and vomiting was not found in any of the three groups.

TWO SEGMENT REGRESSION TIME:

Two segment regression time was significantly prolonged in Group F1 “P”0.0001.

The above observation is similar to one observed by Prof.Naveen Malhotra et al, Ben David et al.

DURATION OF POST OPERATIVE ANALGESIA:

The duration of post operative analgesia was significantly prolonged in Group F1 “P” 0.0001.

RESPIRATORY DEPRESSION:

Previous studies by Bromage et al in 1981, Lan et al 1983 Showed that Fentanyl upto 25µg did not cause delayed respiratory depression.

They concluded that respiratory depression effect is dose dependant and it is unlikely to occur at a dose below 25µg.

In this study the respiratory rate remained unchanged with the base line.

This study delineates the optimal dose of Bupivacaine and Fentanyl without much morbidity in hospital with moderate post operative care.

CONCLUSION

This study is conducted in patients aged 50-75 years. Spinal Bupivacaine was used in variable doses with Fentanyl 25µg to find out the minimum effective dose of bupivacaine with Fentanyl 25µg in elderly patients undergoing endoscopic urological procedures.

In group B 28% of the patients had significant hypotension who needed bolus intravenous fluids and vasopressors.

In group F1 the haemodynamics were stable with significant prolongation of post operative analgesia than other groups.

In group F11 8% of the patients had intra operative discomfort who needed supplemental intravenous analgesia.

From this study it was concluded that addition of Fentanyl 25µg to 5mg of 0.5% Bupivacaine provides reliable and satisfactory surgical anaesthesia with an ideal peak sensory block height, stable haemodynamic status and without any significant adverse effect in elderly patients undergoing endoscopic urologic procedures.

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PROFORMA

Name: Age: Sex: IP No:

Ht: Wt: ASA: Duty anaesthesiologist:

Pre operative status- PR: BP: RR: CVS: RS:

Blood investigations: Hb%: RBS: Urea: Creatinine:

Blood grouping: H/o drug allergy:

Pre medication: inj. Midazolam 2mg Im 45 minutes before surgery.

PARAMETERS OBSERVED

1.Level of sensory block achieved and time:

2.Degree of motor block:

3.PR: BP: RR: Spo2:

4.Any discomfort: Nausea: Vomiting: Pruritus:

5.Level at the end of surgery:

6.Hypotension- >30% fall: Yes/No

7.Bradycardia: <60/mt: Yes/No

8.Incomplete sensory block: Yes/No

9.Pruritus: Yes/No

10.PONV: Yes/No

11.Shivering: Yes/No

12.Sedation score:

13.Duration of procedure:

14.Level at the end of surgery:

15.Two segment regression time:

16.Duration of post operative analgesia:

SEDATION SCORE:

0 – Fully awake

1- Drowsy

2- Drowsy but arousable on touch (or) call

3- Drowsy but arousable on deep stimuli

4- Somnolent

VAS- 0 hr

1 hr

2 hrs

3 hrs

4 hrs

Visual analog scale. 0 – 1 Excellent

2 - 4 Good

5 – 6 Fair

7 - 8 Poor

9 – 10 No relief

Pain score >6- Supplementory analgesia given.

Motor block – assessed by Bromage scale:

0 – Full flexion of knees, feet, able to lift the extended leg.

1- Unable to lift the extended leg. Just able to flex the knees and full flexion of feet possible.

2- Unable to flex the knees but flexion of feet possible.

3- Unable to move the leg(or) feet.

MASTER CHART

S.No	GROUP	AGE	SEX	IP-NO	DM	HT	IHD	COPD	OTHERS	PR	RR	BP.S	BP.D	MSL	TMSL
1	B	50	M	42392	No	Yes	No	No	No	65	23	150	100	7	7
2	B	60	M	44293	Yes	No	No	No	No	96	22	120	80	8	5
3	B	69	M	47256	No	No	No	No	No	96	20	120	80	6	5
4	B	58	M	50429	No	No	No	No	No	86	14	130	80	7	9
5	B	55	M	47471	No	No	No	No	No	78	14	120	80	10	8
6	B	55	M	52156	No	No	No	No	No	95	14	120	70	11	7
7	B	60	M	57144	No	No	No	No	No	90	18	110	80	9	9
8	B	70	M	53116	Yes	No	No	No	No	98	18	120	70	9	7
9	B	51	M	52672	No	No	No	No	Yes	82	12	130	80	10	7
10	B	65	M	50740	Yes	No	No	No	Yes	90	12	110	80	9	7
11	B	58	M	53742	No	No	Yes	No	No	80	12	120	70	10	7
12	B	59	M	51132	No	No	No	No	Yes	92	16	150	80	10	7
13	B	58	M	42191	No	No	No	No	Yes	90	12	110	70	9	5
14	B	57	M	51463	No	No	No	No	No	90	12	110	70	10	8
15	B	75	M	50938	Yes	No	No	No	No	82	12	100	70	11	7
16	B	73	M	53728	No	No	No	No	No	80	14	130	80	10	5
17	B	52	M	56148	No	No	No	No	No	88	14	110	80	9	8
18	B	60	M	55404	No	No	No	No	No	82	14	130	80	10	6
19	B	65	M	46541	No	No	No	No	Yes	90	14	100	80	9	8
20	B	56	F	59241	No	Yes	No	No	No	78	12	120	70	10	8
21	B	51	F	62916	No	No	No	No	No	90	14	100	70	9	7
22	B	54	M	61645	No	No	No	No	No	90	12	120	70	10	7
23	B	65	M	62419	Yes	Yes	No	No	Yes	90	12	150	90	9	6
24	B	60	M	69450	No	No	No	No	No	90	14	130	80	10	8
25	B	69	M	63988	No	No	No	No	Yes	90	12	100	70	9	7

S.No	GROUP	AGE	SEX	IP-NO	DM	HT	IHD	COPD	OTHERS	PR	RR	BP.S	BP.D	MSL	TMSL
1	F I	54	F	44272	No	Yes	No	No	No	70	20	140	90	8	6
2	F I	62	M	49343	No	No	No	No	No	82	16	110	80	9	7
3	F I	60	M	89216	No	Yes	No	No	No	76	14	130	80	8	5
4	F I	62	M	53577	No	Yes	Yes	No	No	92	18	130	80	9	5
5	F I	69	M	57965	No	No	No	No	Yes	86	16	140	90	10	5
6	F I	70	M	22240	No	No	No	No	No	80	14	110	70	9	5
7	F I	60	M	23379	No	No	No	No	No	84	14	120	80	9	6
8	F I	57	M	48019	No	No	No	No	No	76	12	130	80	10	8
9	F I	76	M	55534	No	No	No	No	No	80	12	120	70	9	6
10	F I	60	M	56158	Yes	No	No	No	No	90	12	130	80	8	6
11	F I	60	M	56149	No	No	No	No	Yes	80	12	110	70	11	5
12	F I	53	M	59391	No	No	No	Yes	No	90	12	120	80	11	6
13	F I	62	M	42623	No	Yes	No	No	No	78	14	130	80	9	6
14	F I	65	M	40164	No	No	No	No	No	86	12	110	70	10	7
15	F I	66	M	40223	No	No	No	No	No	80	14	120	70	9	6
16	F I	52	M	28882	No	No	No	No	No	90	14	110	80	9	5
17	F I	50	M	28259	No	No	No	No	No	68	14	120	70	10	7
18	F I	60	M	38639	No	No	No	No	No	82	14	100	70	9	6
19	F I	50	M	65288	No	Yes	No	No	No	87	18	140	80	9	5
20	F I	60	M	64647	No	No	No	No	No	82	14	120	80	10	5
21	F I	65	M	62892	No	No	No	Yes	No	86	13	140	90	8	7
22	F I	60	M	55454	No	No	No	No	No	80	14	130	80	10	7
23	F I	52	M	66488	No	No	No	No	Yes	86	12	120	90	10	5
24	F I	53	M	66469	No	No	No	No	No	78	14	120	80	8	7
25	F I	66	M	68954	No	No	No	No	No	84	14	130	90	10	7

S.No	GROUP	AGE	SEX	IP-NO	DM	HT	IHD	COPD	OTHERS	PR	RR	BP.S	BP.D	MSL	TMSL
1	F II	60	M	486841	No	No	No	No	No	78	16	150	100	10	7
2	F II	75	M	5820	No	No	No	No	No	82	16	130	80	10	5
3	F II	54	M	6645	No	No	No	No	No	76	12	100	80	10	6
4	F II	50	M	12686	No	No	No	No	No	88	13	120	80	10	7
5	F II	75	M	1446	No	No	No	No	No	70	12	130	80	10	6
6	F II	65	M	7482	Yes	No	No	No	No	80	12	120	70	9	6
7	F II	55	M	4620	No	No	No	Yes	No	76	12	120	70	10	5
8	F II	65	M	10775	No	No	No	No	No	90	14	120	70	10	5
9	F II	50	F	1007	No	No	No	No	No	80	12	120	70	9	7
10	F II	59	F	4307	No	No	No	No	No	90	12	120	70	10	6
11	F II	60	M	12692	No	No	No	No	No	70	18	120	70	8	7
12	F II	60	M	2430	Yes	No	No	No	No	82	18	130	80	10	7
13	F II	60	F	15062	No	No	No	No	Yes	90	14	130	80	10	6
14	F II	79	M	20134	No	Yes	No	No	No	80	14	130	90	10	5
15	F II	74	M	28837	Yes	Yes	No	No	No	92	18	120	80	8	5
16	F II	65	M	20506	No	No	No	No	No	76	14	120	80	10	6
17	F II	65	M	258604	No	No	No	No	No	80	16	130	80	10	5
18	F II	60	M	21651	No	No	No	No	No	70	12	120	70	10	7
19	F II	50	M	28236	No	No	No	No	No	86	12	130	80	10	7
20	F II	69	M	25294	No	No	No	No	No	86	12	120	80	10	6
21	F II	62	M	28884	No	No	No	No	No	70	14	130	80	9	7
22	F II	65	M	47407	No	Yes	No	No	No	88	16	120	80	10	7
23	F II	62	M	48405	Yes	No	No	No	No	93	18	130	80	10	6
24	F II	51	M	49091	No	No	No	No	No	90	14	120	70	9	7
25	F II	70	M	43123	No	No	No	No	Yes	80	12	130	80	10	6

MASTER CHART(continued)

S.No	GROUP	IP-NO	5 .PR	5 S.BP	10PR	10SBP	15PR	15SBP	ISB	RR	NV	PRURITUS	SEDATION SCORE	ANY DIS	DURATION OF PROCEDURE
1	B	42392	96	100	94	120	94	130	No	22	No	No	0	No	20
2	B	44293	74	120	70	120	72	120	No	18	No	No	1	No	35
3	B	47256	74	90	72	100	74	100	No	18	No	No	0	No	25
4	B	50429	90	100	90	110	92	110	No	12	No	No	0	No	25
5	B	47471	80	120	82	120	82	120	No	12	No	No	0	No	25
6	B	52156	98	110	96	110	96	110	No	12	No	No	1	No	20
7	B	57144	100	130	90	130	90	120	No	14	No	No	0	No	30
8	B	53116	80	110	80	110	82	110	No	14	No	No	1	No	20
9	B	52672	90	120	92	120	92	120	No	14	No	No	0	No	35
10	B	50740	92	80	94	100	94	100	No	12	No	No	0	No	50
11	B	53742	100	110	96	110	96	120	No	12	No	No	0	No	45
12	B	51132	94	130	92	130	92	130	No	18	No	No	0	No	30
13	B	42191	86	80	94	100	90	100	No	14	No	No	0	No	35
14	B	51463	96	90	90	100	90	110	No	12	No	No	0	No	25
15	B	50938	90	90	100	100	90	100	No	14	No	No	0	No	45
16	B	53728	90	90	92	98	84	110	No	14	No	No	0	No	40
17	B	56148	90	80	96	100	96	100	No	14	No	No	0	No	20
18	B	55404	86	100	90	110	90	110	No	14	No	No	0	No	25
19	B	46541	80	80	82	100	86	100	No	12	No	No	0	No	40
20	B	59241	88	100	90	110	96	110	No	14	No	No	0	No	30
21	B	62916	92	80	90	100	90	100	No	14	No	No	0	No	25
22	B	61645	84	110	90	110	90	110	No	14	No	No	0	No	30
23	B	62419	94	140	90	130	90	130	No	14	No	No	0	No	60
24	B	69450	91	116	90	120	94	120	No	12	No	No	0	No	30
25	B	63988	86	90	90	100	90	90	No	12	No	No	0	No	35

S.No	GROUP	IP-NO	5 .PR	5 S.BP	10PR	10SBP	15PR	15SBP	ISB	RR	NV	PRURITUS	SEDATION SCORE	ANY DIS	DURATION OF PROCEDURE
1	F I	44272	100	130	84	110	86	110	No	16	No	No	2	No	40
2	F I	49343	78	110	80	110	80	110	No	18	No	No	1	No	40
3	F I	89216	80	100	84	110	80	110	No	12	No	No	1	No	35
4	F I	53577	86	120	90	120	90	120	No	17	No	No	2	No	25
5	F I	57965	92	140	90	120	90	130	No	14	No	No	2	No	45
6	F I	22240	90	100	92	100	90	100	No	14	No	No	1	No	40
7	F I	23379	86	120	90	110	90	110	No	12	No	No	1	No	45
8	F I	48019	84	120	90	120	86	120	No	12	No	Yes	1	No	40
9	F I	55534	70	110	80	110	80	120	No	12	No	Yes	2	No	45
10	F I	56158	96	120	90	120	90	110	No	12	No	Yes	3	No	50
11	F I	56149	90	100	92	100	92	100	No	14	No	Yes	2	No	40
12	F I	59391	90	130	92	120	92	130	No	14	No	No	1	No	40
13	F I	42623	86	120	84	120	86	110	No	14	No	No	1	No	60
14	F I	40164	76	110	80	110	80	110	No	14	No	No	1	No	50
15	F I	40223	86	110	80	110	80	120	No	12	No	No	1	No	30
16	F I	28882	92	110	90	110	90	110	No	14	No	No	1	No	25
17	F I	28259	80	110	84	120	84	120	No	12	No	Yes	1	No	20
18	F I	38639	86	110	84	110	86	110	No	14	No	No	1	No	25
19	F I	65288	88	130	90	130	80	120	No	12	No	No	3	No	60
20	F I	64647	83	110	84	110	86	110	No	12	No	Yes	1	No	40
21	F I	62892	70	120	80	130	80	130	No	14	No	No	1	No	30
22	F I	55454	86	120	84	130	84	130	No	12	No	No	0	No	40
23	F I	66488	80	120	84	110	86	110	No	14	No	No	0	No	30
24	F I	66469	64	110	70	110	70	110	No	12	No	No	1	No	40
25	F I	68954	78	150	80	140	80	140	No	12	No	No	1	No	50

S.No	GROUP	IP-NO	5 .PR	5 S.BP	10PR	10SBP	15PR	15SBP	ISB	RR	NV	PRURITUS	SEDATION SCORE	ANY DIS	DURATION OF PROCEDURE
1	F II	486841	74	130	78	130	78	130	No	20	No	No	1	No	70
2	F II	5820	84	120	84	120	86	120	No	14	No	No	0	No	40
3	F II	6645	84	100	86	100	86	100	No	12	No	No	1	No	50
4	F II	12686	90	120	92	120	92	120	No	14	No	Yes	1	No	60
5	F II	1446	76	120	78	120	76	130	No	12	No	No	2	No	60
6	F II	7482	86	110	88	110	86	110	No	12	No	No	1	No	55
7	F II	4620	80	120	82	110	82	110	No	12	No	No	2	No	60
8	F II	10775	80	120	84	100	80	100	No	14	No	No	1	No	65
9	F II	1007	80	120	86	120	86	120	No	14	No	No	1	No	40
10	F II	4307	90	120	92	120	92	120	No	14	No	No	1	No	25
11	F II	12692	88	120	90	100	90	110	Yes	16	No	No	0	No	60
12	F II	2430	84	120	80	140	80	130	No	18	No	Yes	0	No	70
13	F II	15062	100	140	90	130	90	130	No	12	No	No	1	No	60
14	F II	20134	86	120	80	120	80	120	No	14	No	No	2	No	65
15	F II	28837	96	100	90	100	90	110	No	20	No	No	2	No	60
16	F II	20506	86	110	84	110	84	110	No	12	No	No	1	No	60
17	F II	258604	82	120	82	120	80	120	No	14	No	Yes	1	No	40
18	F II	21651	80	110	82	110	84	130	No	14	No	No	2	No	60
19	F II	28236	80	120	82	120	82	130	No	14	No	No	1	No	55
20	F II	25294	80	120	80	120	82	110	No	14	No	Yes	1	No	50
21	F II	28884	90	110	92	110	92	120	No	14	No	No	1	No	45
22	F II	47407	113	130	100	130	90	120	Yes	18	No	No	1	No	75
23	F II	48405	102	110	90	100	90	120	No	20	No	No	2	No	55
24	F II	49091	80	110	80	100	80	110	No	14	No	No	1	No	25
25	F II	43123	84	120	86	130	86	130	No	12	No	No	1	No	50

ABBREVIATIONS

DM - Diabetes Mellitus

HT - Hyper Tension

IHT - Ischeamic Heart Disease

COPD- Chronic Obstructive Pulmonary Disease

PR - Pulse Rate

RR - Respiratory Rate

BP-S - Blood Pressure Systolic

BP-D - Blood Pressure Diastolic

MSL - Maximum Sensory Level

TMSL- Time of Maximum Sensory Level

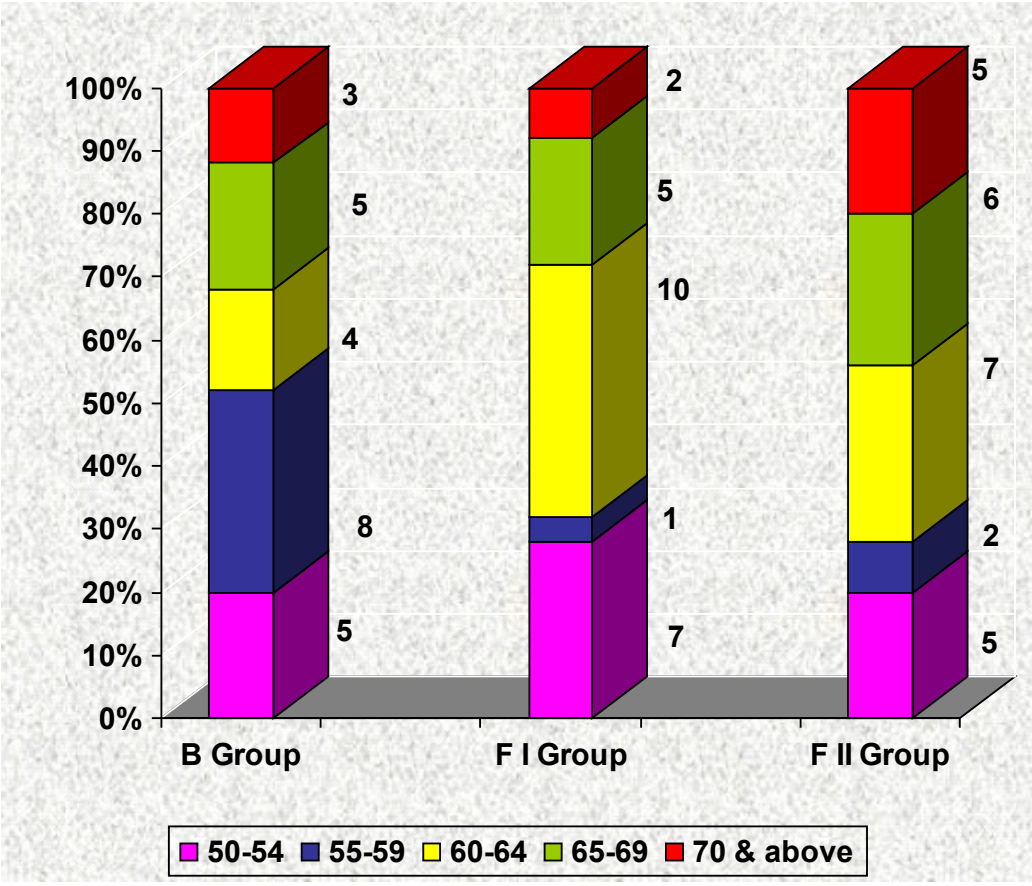
GMB - Grading of Motor Block

ISB - Incomplete Sensory Block

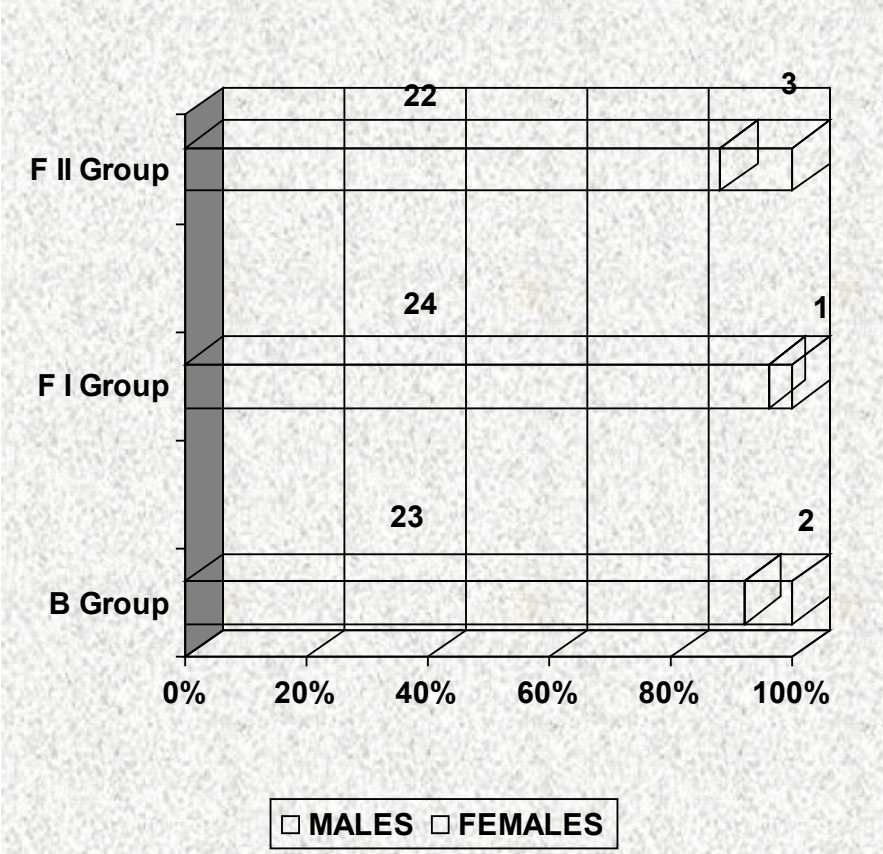
NV - Nausea, Vomiting

2 SR Time - Two segment Regression Time

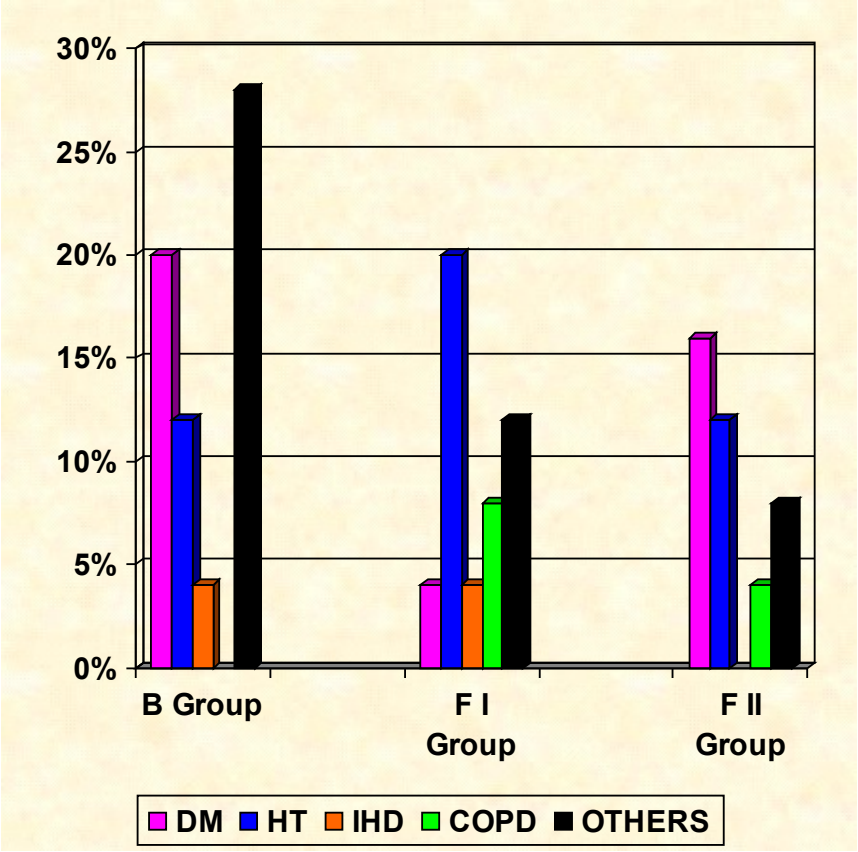
AGE DISTRIBUTION



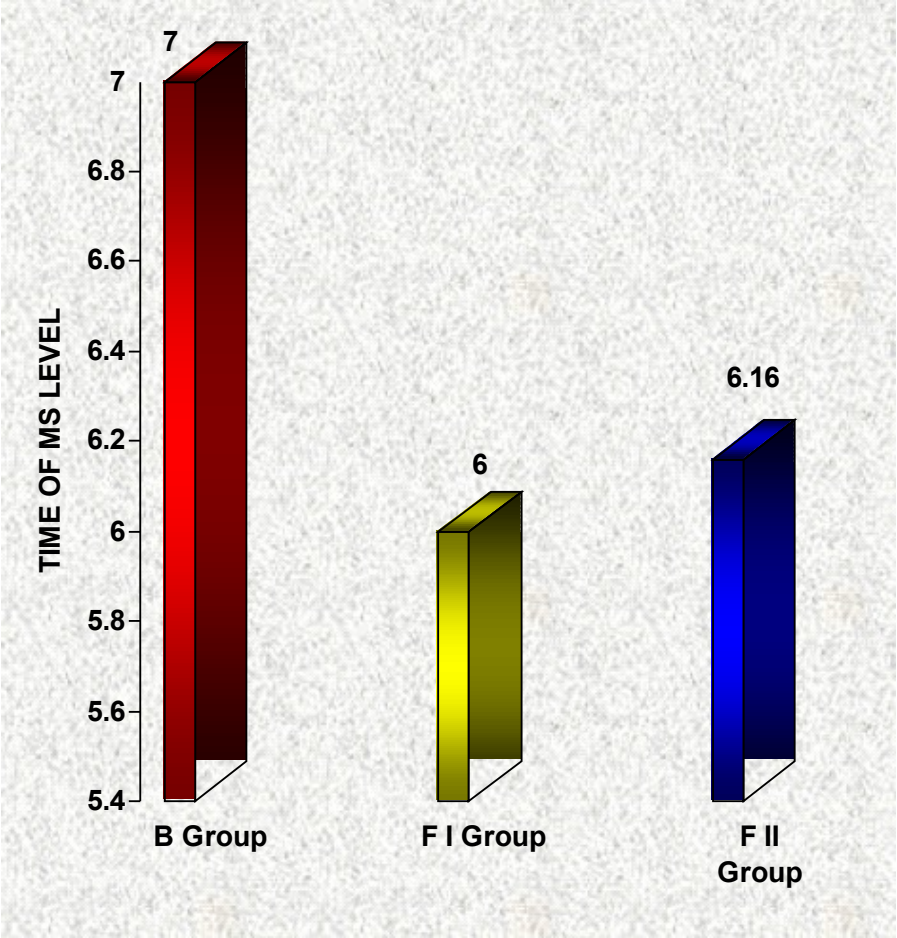
SEX DISTRIBUTION



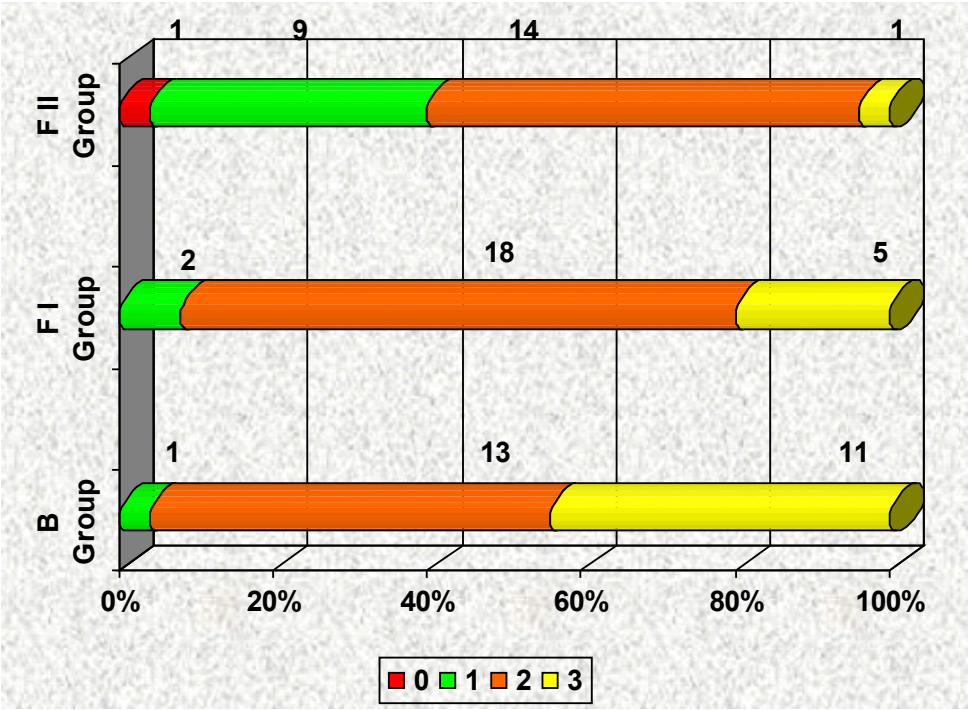
HISTORY OF ILLNESS



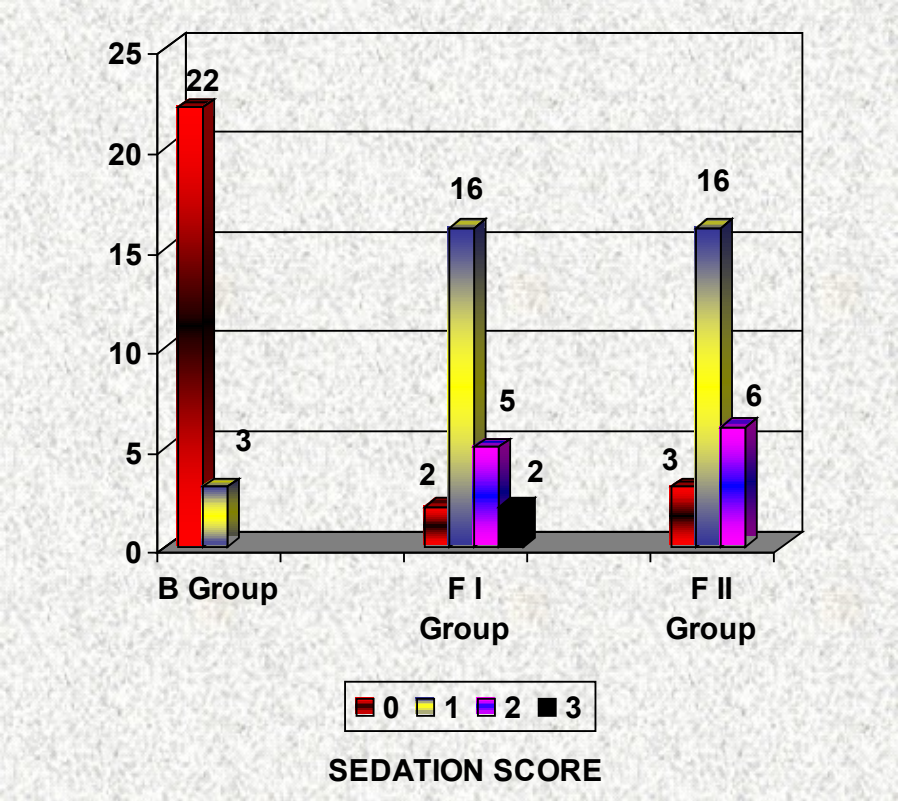
TIME OF MAXIMUM SENSORY LEVEL



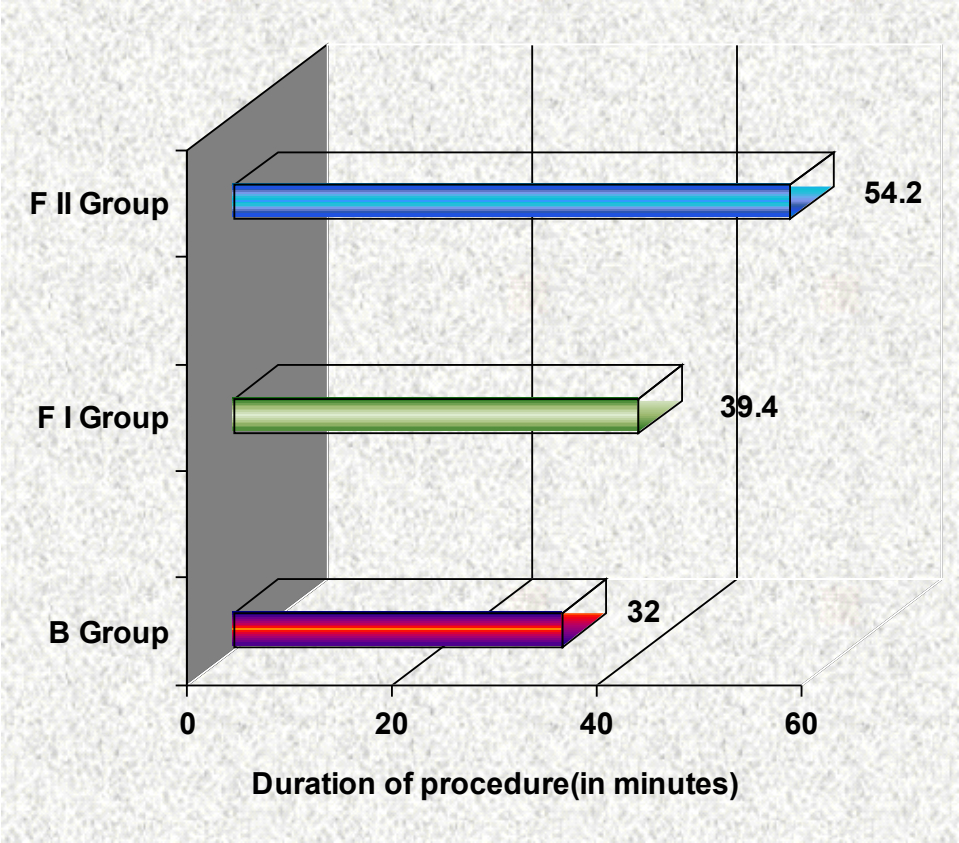
GRADING OF MOTOR BLOCK



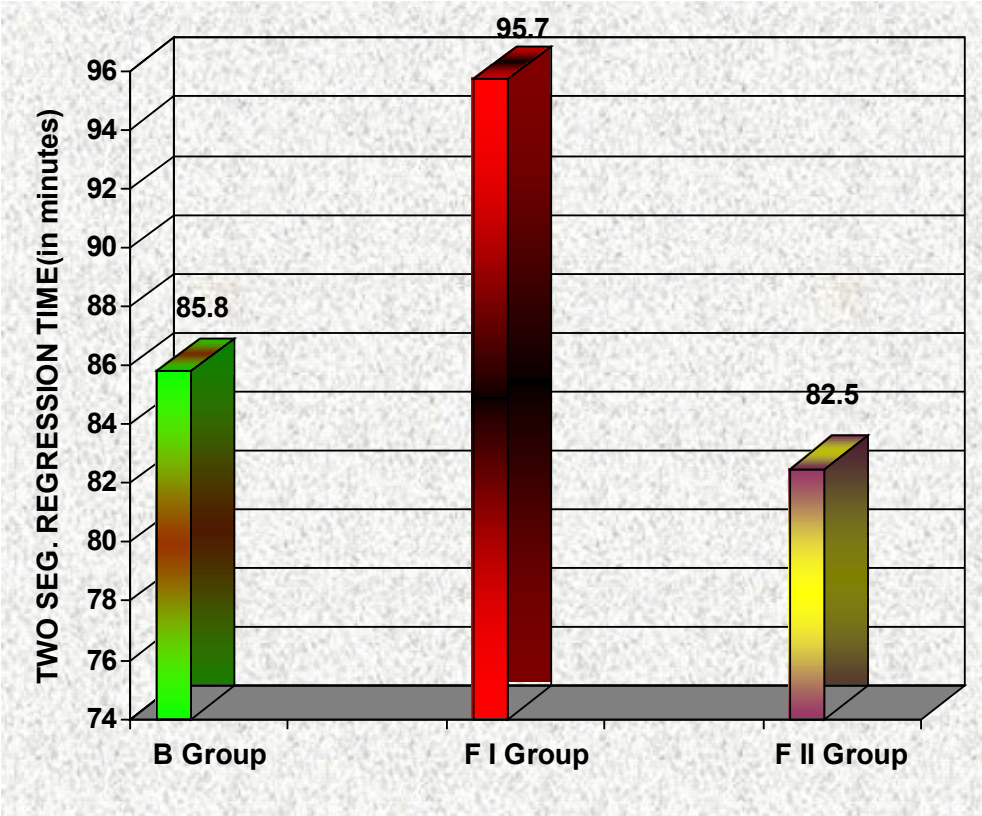
SEDATION SCORE



DURATION OF PROCEDURE



TWO SEGMENT REGRESSION TIME



DURATION OF POST OPERATIVE ANALGESIA